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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,020	01/23/2001	Ralph J. Greenspan	066655-0026	9299

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
12/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mweipdocket@mwe.com
SIP_Docket@mwe.com

Office Action Summary	Application No.	Applicant(s)	
	09/768,020	GREENSPAN ET AL.	
	Examiner	Art Unit	
	James (Doug) Schultz, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,23 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 23, 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed September 22, 2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed March 22, 2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments, Claim Rejections - 35 USC § 112

Claims 22, 23, and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for reasons of record, and applicant's arguments are responded to below.

Applicants traverse the rejection of claims 22, 23 and 27-29 under 35 U.S.C. § 112, first paragraph, as lacking written description of the claimed invention sufficient to show that the inventors were in possession of the invention at the time the application was filed.

At the outset, it is noted that claim 1 specifically requires that any compound that is found capable of producing any altered phenotype when administered to any animal containing a mutation in any one of 13 different recited genes, most if not all of which are found exclusively

in Drosophila, is necessarily required to be a therapeutic agent for treating Alzheimer disease. Accordingly, in order for the claim to be properly supported under 35 USC 112, the specification is required to demonstrate possession of an animal model that is representative of Alzheimer's disease. Without this, one of skill would be unable to perform the claimed method towards the claimed the end of identifying agents that are therapeutic for treating Alzheimer's disease. It is the demonstration of possession of such an animal model in which the instant specification is considered to be lacking.

Applicants have argued that the specification teaches that an "Alzheimer's disease gene" can be a gene that is differentially expressed at the mRNA or protein levels in $Appl^{d}$ flies as compared to $Appl^{+}$ flies, and that tables 4-6 discloses several dozen examples thereof. However, the designation of the genes in tables 4-6 as "Alzheimer's disease genes" appears to be made independent of whether these genes are actual therapeutic targets in the treatment of Alzheimer's disease in humans, since the genes listed in claim 1 are specific to Drosophila (fruit flies). Applicants note that these genes were identified based upon differential expression in Drosophila, and the specification teaches that some of these Drosophila genes have homology with some human, rat or mouse genes that are thought to be involved in the development of Alzheimer's disease.

In response, differential expression and homology are considered insufficient to define a gene as an "Alzheimer's disease gene" in the sense that such a gene is a legitimate target in a therapy for treating Alzheimer's disease, for multiple reasons. Alzheimer's disease is a human disease and does not exist in Drosophila, and genes that are differentially expressed in Drosophila could not be expected to be the same genes that might be differentially expressed in a

human having Alzheimer's disease. Furthermore, the term "homology" means only that they share some structural similarities. One of skill in the art would understand that there may or may not be shared function between homologous genes, particularly those that reside in species as different from each other as humans and Drosophila. Moreover, the context in which the denoted "differential expression" was measured in the specification was in response to deletion of amyloid precursor like protein (appl) in Drosophila. While appl shares homology with the human amyloid precursor protein (APP), homology in one of skill in the art would understand that knocking out APP in a human (if technically/ethically feasible) would not predictably result in the upregulation of homologous genes as those that are upregulated in response to appl in Drosophila, since the physiological environment in which appl is present (i.e. Drosophila neurons) is different from the physiological environment in which APP is present (i.e. human neurons). Since claim 1 is directed to screening for therapeutics that target Alzheimer's disease, which is necessarily in humans, compounds that inhibit mutated version of one of the 13 gene recited in claim 1 in Drosophila could not be expected to predictably inhibit the "homologous" human gene, let alone achieve inhibition sufficient to result in compounds that treat a disease as intractable as Alzheimer's, even if the homologous gene were a legitimate target in the treatment of Alzheimer's disease.

Thus, the argument that the specification teaches possession of the genus of parental strains that carry a mutation in an Alzheimer's disease gene is not convincing, since Applicants have defined an "Alzheimer's disease gene" in such a manner to include genes that are not actually therapeutic targets for treating Alzheimer's disease. Should applicants disagree, a

showing is requested that demonstrates how identifying an inhibitor of Suppressor of Hairless (from claim 1 for example) would necessarily treat Alzheimer's disease as required and claimed.

Applicants point out that, while the methods of the invention are exemplified using the genetic system Drosophila, that any genetic system suitable for transmission genetics and convenient analysis of test and sibling control progeny is useful for practicing the methods of the invention (page 17, lines 1-10). Applicants point to the specification as further describing that examples of genetic systems suitable for practicing the methods of the invention include, for example, mice, zebrafish, nematodes, and yeast (page 17, lines 1-10). However, it is not clear that the genes listed in claim 1 are found in any of the above listed species beyond Drosophila. The examiner is unable to locate any reference that teaches the expression of the "mastermind" (claim 1) gene in mice, for example.

The argument that the specification teaches a variety of behavioral, morphological and other physical phenotypes useful in the methods of the invention is similarly unconvincing. The specification includes a prophetic list of traits that allegedly comprise phenotypes that are testable in identifying Alzheimer's therapeutics, including, Drosophila eye color, wing shape, bristle appearance, size, phototaxis and viability, as well as the size, viability, eye color, coat color, or exploratory behavior of mice; the size, viability, skin color, or optomotor response of zebrafish; the size, viability, phototaxis or chemotaxis of nematodes; and the colony color, colony size or growth requirements of yeast. In response, the examiner is unable to identify any art-recognized relationship that suggests that a molecule discovered by the method of claim 1 that is capable of altering "bristle appearance" (for example) in Drosophila will also predictably comprise a therapeutic for Alzheimer's disease in a non-Drosophila species.

Claims 22, 23, and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for reasons of record, and applicant's arguments are responded to below.

Applicants have traversed the instant rejection in much the same manner as discussed above. Applicants allege that the specification teaches a variety of behavioral, morphological and other physical phenotypes that are useful in the present methods. Applicants assert that viability is a particularly useful phenotype for establishing a fund to functional interaction between genes and point to example 1 in support. In response, it is acknowledged that the specification lists numerous phenotypes and genes that may serve as a basis for investigating a relationship between the two. However, the claim is not directed to investigating such a relationship, but rather is drawn to the requirement that any putative relationship would necessarily allow one of skill to produce a compound that treats Alzheimer's disease. It is maintained that even if one of skill were able to exploit the knowledge of a relationship between a Drosophila-specific gene and its phenotype to produce a chemical modulator of this phenotype, that a therapeutic for Alzheimer's disease would not be the predictable result. The combination of the prior art and the instant specification is considered to be silent as to how to predictably use the discovery of a chemical modulator of a Drosophila specific gene and its resulting altered phenotype to extrapolate to treatment of a human specific disease, i.e. Alzheimer's disease. The rejection is maintained therefore.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James (Doug) Schultz, PhD whose telephone number is (571)272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James (Doug) Schultz, PhD/
Primary Examiner, Art Unit 1633